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FISH & NEAVE IP GROUP
ROPES & GRAY LLP
ONE INTERNATIONAL PLACE
BOSTON, MA 02110-2624

EXAMINER

HOWARD, ZACHARY C

| ART UNIT | PAPER NUMBER |
|----------|--------------|
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1646

DATE MAILED: 10/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No. .

09/977,864

Applicant(s)

DUDEK ET AL.

Examiner

Zachary C. Howard

Art Unit

1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 July 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-21 and 23-25 is/are pending in the application.
- 4a) Of the above claim(s) 4,6-16 and 18-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3,5,17,21 and 23-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1,3-21 and 23-25 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 15 April 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 12/9/05;2/8/06;4/3/06.

- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

Art Unit: 1646

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendments of 4/3/06 and 7/28/06 have been entered in full. Claims 1, 3, 5 and 21 are amended. Claims 2 and 22 are canceled. New claims 23-25 are added, and are considered to be drawn to the elected invention (Group I) and encompass the elected species (colon cancer and hedgehog antibody).

Claims 4, 6-16 and 18-20 remain withdrawn as from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention or a non-elected species. This application contains claims 10-16, 19 and 20 drawn to an invention nonelected with traverse in Applicant's response filed 9/14/05. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 1, 3, 5, 17, 21 and 23-25 are under consideration in the instant application, as they read upon the elected species of colon cancer and hedgehog antibody.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

The Information Disclosure Statements of 12/9/05, 2/8/06 and 4/3/06 have each been considered in full.

Oath/Declaration

The 11/2/2005 Office Action (pg 4) indicated that the instant application did not contain a properly executed declaration. In response, Applicants have indicated that an executed declaration was mailed 1/14/2002 in reply to a notice of missing parts. Applicants submit a copy of the previously submitted declaration. The Examiner has fully considered this copy of the declaration and finds it sufficient.

Art Unit: 1646

Withdrawn Objections and/or Rejections

The following page numbers refer to the previous Office Action (11/2/05).

All objections and/or rejections of claims 2 and 22 are moot in view of Applicants' cancellation of these claims.

The objection to claim 21 at pg 4 is *withdrawn* in view of Applicants' amendments to the claims.

The rejection of claims 1, 3, 5, 17 and 21 under 112, first paragraph at pg 4-9, as lacking enablement for the full scope of the claims is *withdrawn* in view of Applicants' amendments to the claims, Applicants' persuasive arguments at pg 7-11 of the 4/3/06 response, and further consideration by the Examiner.

The rejection of claim 1, 3, 5, 17 and 21 at pg 12 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is *withdrawn* in view of Applicants' persuasive arguments at pg 12-13 of the 4/3/06 response.

The rejection of claims 1-3, 5, 17 and 21 under 35 U.S.C. § 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps, is *withdrawn* in view of the Applicants' persuasive arguments at pg 13 of the 4/3/06 response.

The rejection of claims 1-3 and 17 under 35 U.S.C. § 102(a) as anticipated by Taipale et al (2000) at pg 13 is *withdrawn* in view of Applicants' amendments to the claims to limit the claims to methods of using a hedgehog antibody.

The rejection of claims 1-3 and 17 under 35 U.S.C. § 102(e) as anticipated by Baxter et al (U.S. Patent 6,545,005), at pg 13-14 is *withdrawn* in view of Applicants' amendments to the claims to limit the claims to methods of using a hedgehog antibody.

The rejection of claims 1-3 under 35 U.S.C. § 102(e) as anticipated by Scott et al (U.S. Patent 6,429,354) at pg 14-15 is *withdrawn* in view of Applicants' amendments to the claims to limit the claims to methods of using a hedgehog antibody.

Art Unit: 1646

The rejection of claim 5 under 35 U.S.C. § 103(a) as being unpatentable over Scott et al (U.S. Patent 6,429,354) at pg 15-16 is *withdrawn* in view of Applicants' amendments to the claims to limit the claims to methods of using a hedgehog antibody.

Maintained Objections and/or Rejections

Claim Objections

Claim 17 is objected to because the claim encompasses non-elected species. This objection was set forth at pg 4 of the 11/2/05 Office Action.

In 4/3/06 response, Applicants argue that the election of species was made for search purposes only, and that upon allowance of a generic claim, Applicants will be entitled to a rejoinder of the claim.

This argument has been fully considered but is not found persuasive. Claim 17 encompasses a variety of species of hedgehog antagonists, including small molecules and antibodies. Claim 17 has been amended to depend from claims "1 and 2-9" (it is noted that claim 2 is canceled). However, claim 1 (and dependent claims 3-9) has been amended by Applicants to be limited to a method of using a hedgehog antibody, and does not include the other species recited in dependent claim 17.

Claim Rejections - 35 USC § 112, 1st paragraph, written description

Claims 1, 3, 5, 17, 21 and 23-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection was set forth at pg 9-11 of the 11/2/05 Office Action for claims 1, 3, 5, 17 and 21; new claims 23-25 are herewith included in this rejection.

Art Unit: 1646

In the response dated 4/3/06, Applicants submit the claims have been amended to limit the hedgehog antagonists to hedgehog antibodies (pg 12). Applicants request reconsideration and withdrawal of this rejection in view of the claim amendments.

Applicants' arguments have been fully considered but are not found persuasive. The rejection set forth 11/2/05 stated that only a "method of using a hedgehog antibody 5E1, or cyclopamine, to inhibit unwanted cell proliferation of a pancreatic, bladder, prostate, lung or colon cancer cell line overexpressing the gli1 or Shh genes, either (1) in vitro or (2) subcutaneously injected in a mammal, but not the full breadth of the claim meets the written description provision". In response, Applicants have narrowed the claims from methods of using "hedgehog antagonists" to methods of using "hedgehog antibodies". In view of these amendments, the Examiner has considered the written description rejection with respect to a hedgehog antibody. However, the specification does not provide a description of the genus of antibodies that are encompassed by the term "hedgehog antibody" and that will function to inhibit unwanted cell proliferation.

The specification teaches "the term "hedgehog" is used to refer generically to any member of the hedgehog family, including sonic, indian, desert and tiggy winkle. The term may be used to indicate protein or gene" (pg 17). The specification further describes a variety of hedgehog mutant proteins (pg 81-88). In view of the teachings of the specification, the term "hedgehog antibody" encompasses a genus of antibodies that includes monoclonal or polyclonal antibodies to any variant of a Sonic, Indian, Desert, or Tiggy-winkle protein or nucleic acid. Said genus is highly variant because a significant number of structural differences are permitted between the molecules (proteins or nucleic acids) to which the antibodies are generated, and therefore between the generated antibodies themselves. The claims do not require that the antibodies possess any particular conserved structure or function, or other disclosed distinguishing feature other than the ability to inhibit "unwanted cell proliferation". The instant specification fails to describe the entire genus of hedgehog antibodies that will work with the claimed inventions.

Art Unit: 1646

From the specification, it is clear that Applicants has possession of a method of inhibiting proliferation of several cancer cell lines (e.g., prostate or colon) that are subcutaneously injected in a mammal, by using the hedgehog monoclonal Sonic hedgehog 5E1 antibody. The 5E1 antibody is described in the prior art as being a monoclonal antibody to the N-terminal fragment of the Sonic hedgehog (Shh) protein. Therefore, Applicants describe a single monoclonal antibody to the N-terminal fragment of Shh protein that works in the claimed method. Applicants do not describe the epitope on the N-terminal fragment of Shh protein to which the 5E1 antibody reacts. Applicants do not describe any other monoclonal or polyclonal antibody to Shh protein, or a variant of Shh protein, that will function to inhibit unwanted cell proliferation. Applicants do not describe any antibodies to Indian, Desert, Tiggy-winkle proteins that function to inhibit unwanted cell proliferation. Applicants do not describe any antibodies to hedgehog nucleic acids that inhibit unwanted cell proliferation.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide sufficient descriptive information, such as definitive structural or functional features, or critical conserved regions, of the genus of hedgehog antibodies to be used in the claimed methods. There is not even identification of any particular portion of the structure that must be conserved. Structural features that could distinguish antibodies in the genus are missing from the disclosure. There is no information regarding the relation of structure to function. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the antibodies

Art Unit: 1646

encompassed. Thus, no identifying characteristics or properties of the instant polypeptides are provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicants were not in possession of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of hedgehog antibodies that would work to inhibit proliferation of cancer cells, or treat cancer, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGFs were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only a method of using a hedgehog monoclonal antibody 5E1 to inhibit unwanted cell proliferation of cells overexpressing the *gli-1* gene, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first

Art Unit: 1646

paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see pg 1115).

Double Patenting

Claims 1, 3, 5, 17, 21 and 23-25 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 5, 17, 21 and 22 of copending Application No. 10/652298. Although the conflicting claims are not identical, claims 1, 3, 5, 17 and 21 are not patentably distinct from each other for the reasons set forth at pg 16-18 of the 11/2/05 Office Action. Each of new claims 23-25 depends from claim 3 or 17 and reads upon the elected species of colon carcinoma. Therefore, each of new claims 23-25 is herewith added to this rejection. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

In the 4/3/06 response, Applicants states their intent to file a terminal disclaimer upon indication of allowable subject matter. The Examiner notes that the provisional double patenting rejection will be withdrawn if a terminal disclaimer is filed; however, the provisional rejection will be maintained until said terminal disclaimer is filed.

New Objections and/or Rejections Necessitated by Applicants' Amendment

Claim Objections

Claims 1, 17 and 21 are objected to because of the following informalities:

(1) In claims 1 and 21, as amended, the word "hedgehog" is not italicized as it is in the previously submitted claims (e.g., claim 17).

(2) Claim 17 depends from canceled claim 2.

Appropriate correction is required.

Art Unit: 1646

Claim Rejections - 35 USC § 112, 2nd paragraph

Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 recites the limitation "said *hedgehog* antagonist" in line 1. There is insufficient antecedent basis for this limitation in the claim. Claim 17 depends from claim 1. Claim 1 has been amended to recite "said hedgehog antibody". In view of this amendment the phrase "said *hedgehog* antagonist" in claim 17 lacks antecedent basis.

Art Unit: 1646

Conclusion

No claims are allowed.

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

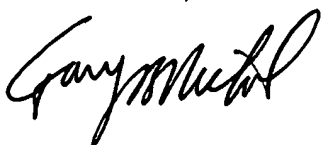
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C. Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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GARY B. NICKOL, PH.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600